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=> file wpids
FILE 'WPIDS' ENTERED AT 14:40:20 ON 20 JUN 96
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FILE LAST UPDATED: 18 JUN 96                    <960618/UP>
>>>UPDATE WEEKS:
MOST RECENT DERWENT WEEK                9624    <199624/DW>
DERWENT WEEK FOR CHEMICAL CODING:       9612
DERWENT WEEK FOR POLYMER INDEXING:      9620
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE
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=> s fox, g?/au or fox g?/au
            30 FOX, G?/AU
            30 FOX G?/AU
L1          30 FOX, G?/AU OR FOX G?/AU

=> s ciossek, t?/au or ciossek t?/au
             0 CIOSSEK, T?/AU
             0 CIOSSEK T?/AU
L2           0 CIOSSEK, T?/AU OR CIOSSEK T?/AU

=> s ullrich, a?/au or ullrich a?/au
            33 ULLRICH, A?/AU
            33 ULLRICH A?/AU
L3          33 ULLRICH, A?/AU OR ULLRICH A?/AU

=> s millauer, b?/au or millauer b?/au
             1 MILLAUER, B?/AU
             1 MILLAUER B?/AU
L4           1 MILLAUER, B?/AU OR MILLAUER B?/AU

=> s kinase?
L5        1484 KINASE?

=> s l1 and l5
L6           1 L1 AND L5

=> s l5 and (l3 or l4)
L7          12 L5 AND (L3 OR L4)

=> d l6 bib,abs 1

L6   ANSWER 1 OF 1  WPIDS   COPYRIGHT 1996 DERWENT INFORMATION LTD
AN   95-373799 [48]   WPIDS
DNN  N95-275604       DNC C95-161991
TI   New nucleic acid encoding EPH-like receptor tyrosine kinase
     (s)  - and related vectors, host cells, proteins, antibodies etc.,
     used diagnostically and therapeutically to modulate receptor
     activation or prodn..
DC   B04 D16 S03
IN   FOX, G M; JING, S; WELCHER, A A
PA   (AMGE-N) AMGEN INC
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< Arti Shah- Stic Searcher- 308-4259 >

CYC 62
PI WO 9528484 A1 951026 (9548)* EN 135 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UG UZ VN
AU 9522925 A 951110 (9607)
ADT WO 9528484 A1 WO 95-US4681 950414; AU 9522925 A AU 95-22925 950414
FDT AU 9522925 A Based on WO 9528484
PRAI US 94-229509 940415
AN 95-373799 [48] WPIDS
AB WO 9528484 A UPAB: 960108
An isolated nucleic acid (I) encoding a polypeptide (II) with at least one of the biological activities of an EPH-like receptor protein tyrosine **kinase** (RPTK), is claimed. It has one of 2962, 2162, 3116 or 4529 bp nucleic acid sequences given in the specification (it may also be a complementary strand, hybrid, or degenerate hybrid of these).
USE - Transformed cells are used to express EPH-like RPTK for therapeutic or diagnostic use, including targeted expression in selected tissue. (IIa), esp. in soluble form, can be used to modify endogenous activation of RPTK, while synthesis of these receptors can be modulated by oligonucleotides antisense to (I), e.g. to alter proliferation and/or differentiation of receptor bearing cells. Abs can be used diagnostically to modulate receptor activation, and to isolate cells bearing EPH-like receptors (these are potentially useful in the treatment of patients deficient in specific cell types). (I) or its fragments can be used in hybridisation assays, or to detect genetic abnormalities.
Dwg.0/11

=> d l7 bib,abs 1-12 Is your applicant

L7 ANSWER 1 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 96-077343 [08] WPIDS
DNN N96-064355 DNC C96-025580
TI Treating tyrosine **kinase** signal transduction associated cellular proliferation disorders - by introducing DNA encoding signalling incompetent inositol 1, 4, 5-tri phosphate receptor, which competes with endogenous receptor.
DC B04 D16 S03
IN FISCHER, G A; **ULLRICH, A**
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN
CYC 63
PI WO 9600586 A2 960111 (9608)* EN 126 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TT UA UZ VN
AU 9529789 A 960125 (9617)
WO 9600586 A3 960215 (9622)
ADT WO 9600586 A2 WO 95-EP2532 950629; AU 9529789 A AU 95-29789 950629; WO 9600586 A3 WO 95-EP2532 950629

FDT AU 9529789 A Based on WO 9600586
PRAI US 94-268390 940630
AN 96-077343 [08] WPIDS
AB WO 9600586 A UPAB: 960227
Inhibiting the effects of inositol 1, 4, 5-triphosphate (IP3) receptor-mediated signal transduction by an endogenous IP3 protein in a cell comprises, delivering a DNA molecule encoding a signalling-incompetent (SI) form of the IP3 receptor protein to the cell, so that the SI form is produced and competes with the endogenous receptor for access to molecules in the IP3 receptor protein signalling pathway, which activate, or are activated by the endogenous IP3 receptor protein.
USE - The method of (1) can be used to treat conditions associated with abnormalities in tyrosine **kinase** signal transduction, by administering a cpd. that inhibits IP-3 receptor activity (claimed). The methods of (2) and (3) can be used to detect cpds. capable of modulating IP3 receptor signal transduction, and molecules capable of binding the IP3 receptor, such cpds. molecules and the method of (1) can be used to inhibit inapropriate cell growth associated with tyrosine **kinase** receptor signal transduction abnormalities, including cancer, psoriasis (claimed) and atherosclerosis.
ADVANTAGE - The introduction of SI IP3 receptor mutants to normal cells does not have a negative effect on cell growth or survival, and the suppression of transforming activities is not oncogene specific.
Dwg.0/8

L7 ANSWER 2 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-382959 [49] WPIDS
DNC C95-165522
TI New poly nucleotide(s) encoding megakaryocyte tyrosine **kinase**(s) - used to develop prods. for the treatment and diagnosis of **kinase** related signal transduction abnormalities..
DC B04 D16
IN GISHIZKY, M; SURES, I; **ULLRICH, A**
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (SUGE-N) SUGEN INC
CYC 61
PI WO 9529185 A1 951102 (9549)* EN 82 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU IS JP KE KG KR KZ LK LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TT UA UZ VN
AU 9523625 A 951116 (9608)
ADT WO 9529185 A1 WO 95-US5008 950424; AU 9523625 A AU 95-23625 950424
FDT AU 9523625 A Based on WO 9529185
PRAI US 95-426509 950421; US 94-232545 940422
AN 95-382959 [49] WPIDS
AB WO 9529185 A UPAB: 951211
Isolated polynucleotide (PN) (I) encoding a megakaryocyte **kinase**-1 (MKK1) protein, is claimed. Also claimed are: (1) isolated PNs encoding MKK2 and 3 proteins; (2) a recombinant DNA vector contg. a PN sequence that encodes a MKK1, 2 or 3 protein; (3)

an engineered host cell that contains a recombinant DNA vector as in (2); (4) an antisense molecule contg. a sequence complementary to at least a part of the coding sequence of a MKK1, 2 or 3 protein, which inhibits translation of the MKK1, 2 or 3 mRNA in a cell; (5) an isolated recombinant MKK1, 2 or 3; (6) a fusion protein comprising MKK1, 2 or 3 linked to a heterologous protein or peptide sequence; and (7) a monoclonal antibody (MAb) which binds to an epitope of MKK1, 2 or 3.

USE - The prods. and methods can be used in the treatment and diagnosis of diseases resulting from abnormalities in MKK signal transduction pathways. They can also be used to treat leukaemia and thrombocytopenia, or for the ex vivo culture of megakaryocytes for the autologous treatment of patients receiving chemotherapy, or other therapies which deplete megakaryocytes and platelets.
Dwg.0/14

L7 ANSWER 3 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-366151 [47] WPIDS
DNN N95-270939 DNC C95-159332
TI Treatment of a disease or condition characterised by abnormality in a signal transduction pathway - by disrupting or promoting the interaction in vivo.
DC B04 S03
IN HOBERT, O; JALLAL, B; KOSTKA, G; OBERMEIER, A; **ULLRICH, A**
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN
CYC 63
PI WO 9526983 A2 951012 (9547)* EN 100 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
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AU 9522334 A 951023 (9605)
WO 9526983 A3 960208 (9622)
ADT WO 9526983 A2 WO 95-US3945 950330; AU 9522334 A AU 95-22334 950330; WO 9526983 A3 WO 95-US3945 950330
FDT AU 9522334 A Based on WO 9526983
PRAI US 94-291591 940815; US 94-221642 940331; US 94-251691 940531
AN 95-366151 [47] WPIDS
AB WO 9526983 A UPAB: 951128
Treatment of a disease or condition is claimed, where the disease or condition is characterised by an abnormality in a signal transduction pathway involving the interaction between: (a) a receptor tyrosine **kinase** of the Trk family and a signalling component; (b) a heterogeneous ribonucleoprotein MP domain and a SH3 domain; (c) a MP domain and a vav protein SH3 domain; or (d) a SH3 domain and a DYN domain by disrupting or promoting the interaction in vivo.

USE - The method is useful for screening, diagnosing and treating diseases, such as neurodegenerative or neuroproliferative disorders or cancer (claimed). Screening methods for agents useful to treat such diseases are also provided.
Dwg.0/3

L7 ANSWER 4 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD

AN 95-320318 [41] WPIDS
DNN N95-240968 DNC C95-142264
TI Modulating signal transduction of insulin receptor type tyrosine **kinase** - by inhibiting its de-phosphorylation by reactor protein phospho-tyrosine phosphatase, also methods for identifying inhibitors useful for treating diabetes mellitus.
DC B04 D16 S03
IN KHARITONENKOV, A E; LAMMERS, R; SAP, J M; SCHLESSINGER, J; **ULLRICH, A**
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (UYNY) UNIV NEW YORK STATE
CYC 60
PI WO 9523217 A2 950831 (9541)* EN 74 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AU BB BG BR BY CA CN CZ EE FI GE HU JP KE KG KR KZ LK LR LT LV MD MG MN MW MX NO NZ PL RO RU SD SG SI SK TJ TT UA UZ VN
AU 9519765 A 950911 (9550)
ADT WO 9523217 A2 WO 95-US2619 950228; AU 9519765 A AU 95-19765 950228
FDT AU 9519765 A Based on WO 9523217
PRAI US 94-203189 940228
AN 95-320318 [41] WPIDS
AB WO 9523217 A UPAB: 951019
Modulating signal transduction mediated by an insulin receptor type tyrosine **kinase** (A) comprises inhibiting dephosphorylation of (A) by a receptor protein phosphotyrosine phosphatase (B). Also claimed are: (1) a method for detecting or quantifying complex (C) formed between receptor-type protein tyrosine phosphatase (RPTP) alpha or epsilon and (A); (2) a method for identifying or isolating cpds. able to bind to (C); (3) a method for identifying cpds. that block formation of (C); (4) a method for identifying cpds. that modulate (A)-mediated signal transduction by modulating activity of RPTP alpha or epsilon; (5) compsns. for treating or preventing diabetes mellitus types I and II contg. antisense RPTP alpha or epsilon nucleic acid molecules and a carrier.

USE - Modulation can be used to stimulate or mimic signal transduction. Cpds. identified by method (4) can be used to treat diabetes or (not claimed) other diseases caused by dysfunctional signal transduction by (A). Also contemplated (not claimed) is gene therapy to generate deletion or missense RPTP mutants that interact with (A) but do not function in signal transduction.No dosage is given. Therapeutic cpds. can be administered by injection or orally.

ADVANTAGE - The identified modulators should be of low toxicity since they are specific for (B) associated with the insulin receptor but do not affect other (B). Dephosphorylation of (A) is inhibited even in absence of insulin.

Dwg.0/8

L7 ANSWER 5 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-311540 [40] WPIDS
DNC C95-138756
TI Cell lines useful for the screening and identification of cpds. - through modulation of phospho-tyrosine phosphatase activity and insulin receptor tyrosine **kinase** mediated signal

transduction.
DC B04 D16
IN HOPPE, E; MOLLER, N P H; **ULLRICH, A**
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN
CYC 61
PI WO 9523231 A1 950831 (9540)* EN 38 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SG SI SK TJ TT UA UZ VN
AU 9518125 A 950911 (9550)
ADT WO 9523231 A1 WO 95-EP731 950228; AU 9518125 A AU 95-18125 950228
FDT AU 9518125 A Based on WO 9523231
PRAI US 94-203218 940228
AN 95-311540 [40] WPIDS
AB WO 9523231 A UPAB: 951011
A genetically engineered mammalian cell (I) contains:(a) a first nucleic acid mol. having a nucleotide sequence which encodes a protein phosphotyrosine phosphatase (PTP) or its fragment, operatively associated with an element that controls its expression, and(b) a second nucleic acid mol. which encodes an insulin receptor protein tyrosine **kinase** (IR-PTK), or its fragment, operatively associated with an element that controls its expression, where a PTP and an IR-PTK are co-expressed by the mammalian cell.

Also claimed are: (1) a method for determining whether a cpd. is capable of modulating IR-PTK signal transduction by modulating phosphotyrosine phosphatase activity of receptor protein tyrosine phosphatases alpha (RPTPs) or RPTP epsilon, comprises:(a) contacting the cpd. with a whole live or fixed (I), for an interval sufficient for the cpd. to modulate the signal transduction;(b) measuring the signal transduction, and(c) comparing the signal transduction to that incubated without the cpd.;(2) a method for identifying a nucleic acid mol. encoding a gene product which is capable of modulating IR-PTK signal transduction by modulating the enzymatic activity of phosphotyrosine phosphatase, comprising:(a) introducing the nucleic acid mol. into (I);(b) culturing the cells so that the gene product encoded by the nucleic acid mol. is expressed in the cells and interacts with the phosphotyrosine phosphatase and IR-PTK or its deriv.;(c) measuring the signal transduction, and(d) comparing the signal transduction to that in the cells without the nucleic acid mol., thereby determining whether the gene product encoded by the nucleic acid mol. is capable of modulating signal transduction;(3) a method for isolating from a mixt. the nucleic acid mol. described in (2), comprising steps (a) to (d) from (2), and(e) selecting and culturing the cells identified in (d) and recovering the nucleic acid mol., thereby isolating the nucleic acid mol..

USE - (I) are used to screen and identify non-toxic cpds. that could elicit or modulate insulin signal transduction even in the absence of insulin (claimed), therefore, (I) are useful in screening assays for non-toxic cpds. that, by modulating phosphatase activity, modulate or prolong IR-PTK signal transduction. The methods have uses in the treatment of diabetes.
Dwg.0/3

L7 ANSWER 6 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-263705 [34] WPIDS
DNC C95-120078
TI Treatment of, e.g., cancers, atherosclerosis or fibrotic disorders - by admin. of an inhibitor of platelet derived growth factor receptor.
DC B05
IN BAJOR, T; GAZIL, A; HAIMICHAEL, J; HIRTH, K P; KABBINAVAR, F F; KERI, G; LAMMERS, R; LEVITZKI, A; MANN, E; ORFI, L; SCHWARTZ, D P; SHAWVER, L K; SLAMON, D J; SZEKELY, I; TANG, C P; ULLRICH, A; GAZIT, A
PA (BIOS-N) BIOSIGNAL LTD; (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (SUGE-N) SUGEN INC; (REGC) UNIV CALIFORNIA; (YISS) YISSUM RES & DEV CO
CYC 59
PI WO 9519169 A2 950720 (9534)* EN 15 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA UZ VN
AU 9515633 A 950801 (9546)
WO 9519169 A3 960215 (9622)
ADT WO 9519169 A2 WO 95-US363 950106; AU 9515633 A AU 95-15633 950106; WO 9519169 A3 WO 95-US363 950106
FDT AU 9515633 A Based on WO 9519169
PRAI US 94-179570 940107
AN 95-263705 [34] WPIDS
AB WO 9519169 A UPAB: 950904
Treatment of cell proliferative disorders characterised by inappropriate PDFG-R activity, comprising admin. of a compsn. comprising a cpd. of formula e.g. (I)-(III), or an active drug form or salt of these cpds., which significantly inhibits one or more PDGF-R activities in vitro or in vivo.

In cpds. (I): R1, R2, R2', R2'', R2''' = H, halo, trihalomethyl or NO2; R3 = H, carboxy or carbalkoxy. In cpds. (II): R4, R5 = halo, H, trihalomethyl or NO2; R6 = aryl, alkyl, alkenyl or alkynyl. (c) in cpds. (III): R7, R7', R8 = halo, OH, H, alkoxy, SH, NH or CMe3; R9 = aryl or H.

USE - The cpds. inhibit PDGF-R (platelet derived growth factor receptor) activity and the activity of PDGF-R related **kinases** Flt, Flk and KDR. They may be used to treat cancers (e.g. intra-axial brain cancer, ghoma, ovarian cancer, colon cancer, prostate cancer, lung cancer, Kasposi's sarcoma or melanoma), blood vessel proliferative disorders (e.g. atherosclerosis), or fibrotic disorders (e.g. hepatic fibrotic disorders or mesangial cell proliferative disorders).

Admin. is, e.g., oral, parenteral, or topical. Dosage is 0.02-25 (esp. 0.2-15) mg/kg/day.
Dwg.0/5

L7 ANSWER 7 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-224055 [29] WPIDS
CR 95-224054 [26]

DNN N95-175673 DNC C95-103045
TI New nucleic acid encoding CCK-2 receptor tyrosine **kinase** - and derived vectors, transformed cells, proteins and antibodies, useful for diagnosis and treatment of proliferative and nervous system diseases and for screening modulators.
DC B04 D16 S03
IN ALVES, F H E; **ULLRICH, A**
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN
CYC 58
PI WO 9514089 A2 950526 (9529)* EN 115 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA UZ VN
AU 9481439 A 950606 (9538)
ADT WO 9514089 A2 WO 94-EP3799 941116; AU 9481439 A AU 94-81439 941116
FDT AU 9481439 A Based on WO 9514089
PRAI US 93-153397 931116
AN 95-224055 [29] WPIDS
CR 95-224054 [26]
AB WO 9514089 A UPAB: 950727
Isolated nucleic acid (I) encoding a protein of the CCK-2 family that contains an intracellular tyrosine **kinase** domain (TKD) and an extracellular discoidin I domain (DID) is new. Also new are (1) isolated, esp. cDNA, sequences encoding a CCK-2 protein, including its alternatively spliced isoforms; (2) recombinant DNA vector encoding a CCK-2 protein, or its fusion proteins; (3) engineered host cells contg. these vectors; (4) isolated recombinant CCK-2 receptor protein; (5) fusion protein of CCK2 linked to a heterologous protein or peptide, (6) oligonucleotides that encode an antisense sequence complementary to (I) able to inhibit translation of the CCK-2 gene; (7) monoclonal antibodies (Ab) binding specifically to an epitope or CCK-2; (8) methods for screening and identifying (ant)agonists of CCK-2; (9) recombinant vector encoding a truncated CCK-2 with dominant negative activity, able to inhibit biological activity of CCK-2; (10) engineering cells contg. the vector of (9), and (11) the truncated CCK-2 described in (9). The specification includes a 3157bp cDNA sequence for CCK-2, and the corresp. encoded 855 amino acid protein.

USE - Cells expressing CCK-2 are used to isolate cpds. that inhibit or mimic activity of CCK-2 on cells; such cpds. are potentially useful for treatment of proliferative diseases (e.g. cancer) and nervous system diseases (e.g. Alzheimer's or Parkinson's diseases, multiple sclerosis, muscular dystrophy, etc.). Ab and the antisense sequences can also be used to modulate (esp. reduce) endogenous activity of the CCK-2 receptor, and Ab may also be attached to a cytotoxin or radioisotope for therapeutic use or for in vivo imaging of tumours and metastases. (I) can be used diagnostically to detect abberant gene expression (e.g. in hybridisation tests on biopsy samples). The truncated CCK-2 partic. expressed from a retroviral vector, can also be used to modulate CCK-2 activity.
Dwg.0/7

L7 ANSWER 8 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 95-224054 [29] WPIDS
CR 95-224055 [26]
DNN N95-175672 DNC C95-103044
TI New nucleic acid encoding MCK-10 receptor tyrosine **kinase** - and derived vectors, transformed cells, proteins and antibodies useful for diagnosis and treatment of proliferative disease, esp. cancer, and for screening modulators.
DC B04 D16 S03
IN ALVES, F H E; **ULLRICH, A**
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN
CYC 58
PI WO 9514088 A1 950526 (9529)* EN 94 pp
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU JP KE KG KP KR KZ LK LR LT LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA UZ VN
AU 9481438 A 950606 (9538)
ADT WO 9514088 A1 WO 94-EP3797 941116; AU 9481438 A AU 94-81438 941116
FDT AU 9481438 A Based on WO 9514088
PRAI US 93-153397 931116
AN 95-224054 [29] WPIDS
CR 95-224055 [26]
AB WO 9514088 A UPAB: 950727

Isolated nucleic acid (I) encoding an MCK-10 (mammary carcinoma **kinase**) protein is new. Esp. (I) is cDNA and may encode an alternatively spliced form of the protein. Also new are (1) recombinant DNA vectors comprising a nucleotide sequence encoding an MCK-10 protein or its fusion proteins; (2) engineered host cells contg. the vectors of (1); (3) isolated recombinant MCK-10 receptor protein; (4) fusion proteins comprising MCK-10 linked to a heterologous protein or peptide; (5) oligonucleotides that encode an antisense sequence complementary to (I), able to inhibit translation of the MCK-10 gene; (6) monoclonal antibodies (Ab) binding specifically to an epitope on MCK-10; (7) methods for screening and identifying antagonists of MCK-10 activity; (8) a recombinant vector encoding a truncated MCK-10 with dominant-negative activity, able to inhibit biological activity of MCK-10; (9) engineered cells contg. the vector of (8), and (10) recombinant truncated MCK-10 as described in (8). The specification includes the 3962 bp sequence of (I) encoding MCK-10 and the corresp. derived 919bp protein.

USE - Cells expressing MCK-10 (or the protein itself) are used to isolate cpds. that inhibit biological activity of MCK-10. Such cpds. are potentially useful for treatment of proliferative diseases such as cancer. MCK-10 ligands (e.g. Ab) and the new antisense sequences can also be used to modulate (specifically reduce) endogenous activity of the MCK-10 receptor. Ab may also be attached to a cytotoxin or radioisotope for therapeutic use or for in vivo imaging of tumours and metastases. (I) can be used diagnostically to detect abberant gene expression (e.g. in hydridisation tests on biopsy samples). The truncated MCK-10 partic. when expressed from a retroviral vector, can also be used to modulate MCK-10 activity.
Dwg.2/6

L7 ANSWER 9 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 94-317002 [39] WPIDS
DNC C94-144495
TI Extracellular signal regulated **kinase** (ERK-5) polypeptide - useful for detecting agonists or antagonists for treating e.g. diabetes mellitus, skeletal muscle diseases or Alzheimer's disease..
DC B04 D16
IN LECHNER, C; MOLLER, N P H; **ULLRICH, A**
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN
CYC 53
PI WO 9421781 A2 940929 (9439)* EN 61 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KG KP KR KZ LK LU LV MD MG MN MW NL NO PL PT RO RU SD SE SI SK TJ TT UA UZ VN
AU 9465119 A 941011 (9504)
US 5459036 A 951017 (9547) 25 pp
EP 689588 A1 960103 (9606) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
WO 9421781 A3 941110 (9610)
ADT WO 9421781 A2 WO 94-IB89 940318; AU 9465119 A AU 94-65119 940318; US 5459036 A US 93-29404 930319; EP 689588 A1 EP 94-912664 940318, WO 94-IB89 940318; WO 9421781 A3 WO 94-IB89 940318
FDT AU 9465119 A Based on WO 9421781; EP 689588 A1 Based on WO 9421781
PRAI US 93-29404 930319
AN 94-317002 [39] WPIDS
AB WO 9421781 A UPAB: 941122
A pure polypeptide (A) comprising a sequence corresp. to the extracellular signal regulated **kinase**, ERK-5, or a fragment contg.more than 9 contiguous amino acids is new. Also claimed are: (1) an isolated nucleic acid (I) encoding (A); (2) a nucleic acid probe for detecting the presence of ERK-5, comprising (I) or more than 27 contiguous nucleotides of (I); (3) a kit for detecting the presence of ERK-5 RNA in a sample, comprising one or more container means having disposed within the probe of (2); (4) a recombinant nucleic acid molecule comprising 5'-3', a promoter effective to initiate transcription in a host cell and (I); (5) a recombinant nucleic acid molecule comprising a vector and (I); (6) a recombinant nucleic acid molecule comprising a transcriptional region functional in a cell, sequence complementary to an RNA encoding (A), and a transcription termination region functional in the cell; (7) a cell contg. one of the above recombinant nucleic acids; (8) an organism contg. one of the nucleic acids; (9) an antibody (Ab) with binding affinity to (A) or a binding fragment, and no affinity to ERK-1, ERK-2, ERK-3, or ERK-4; (10) a diagnostic kit contg. (i) a 1st container means contg. the Ab or (9); and (ii) a 2nd container means contg. a conjugate comprising a binding partner of the Ab (pref. monoclonal Ab) and a label; and (11) a hybridoma producing the monoclonal Ab (MAb) or (9).

(A) comprises all or part of the sequence given in the specification (seq. ID 2) pref. more than 9 contiguous amino acids.(I) comprises all or part of the sequence also given (SEQ ID 1) or allelic, mutant or species variations.

USE - The polypeptide is useful for detecting agonists or antagonists for use in a pharmaceutical compsn. (claimed) for

treating diabetes mellitus, skeletal muscle diseases, Alzheimer disease or peripheral neuropathies. The probe of (2) is useful for detecting the presence of ERK-5 RNA in samples. Antibodies directed against the polypeptide are useful for detecting (A) in samples and for measuring the amt. of (A) in samples, by measuring immunocomplexes formed.
Dwg.0/6

ABEQ US 5459036 A UPAB: 951128
Isolated nucleic acid molecule encodes a polypeptide having an amino acid sequence of at least 9 contiguous amino acids having the sequence given in the specification. Polypeptide has the full length ERK-5 amino acid sequence also given in the specification. Also claimed are a nucleic acid probe comprising the isolated nucleic acid molecule, a kit for detecting the presence of ERK-5 RNA; and a transformant cell contg. the nucleic acid.
USE - Detecting the presence of ERK-5 RNA in a sample. Acting as agonist or antagonist for ERK-5 associated activity, e.g. for treating diabetes mellitus skeletal muscle disorders, Alzheimer's disease and peripheral neuropathies. Dosage is 0.001-50 (0.1-1.0) mg/kg given once or more per day. Admin. is parenteral by injection or infusion e.g. intravenous, intraperitoneal, intramuscular or subcutaneous.
Dwg.0/8

L7 ANSWER 10 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 94-183501 [22] WPIDS
DNN N94-144837 DNC C94-083203
TI DNA encoding Flk-1, a tyrosine **kinase** receptor for vascular endothelial growth factor - used to express recombinant Flk-1 for screening for ligands useful for modulating vasculogenesis and anglogenesis e.g. for treating cancer.
DC B04 D16 S03
IN **MILLAUER, B**; RISAU, W; **ULLRICH, A**
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN; (PLAC) MAX PLANCK SCI PROMOTION INST
CYC 40
PI WO 9411499 A1 940526 (9422)* 99 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
W: AU BG BR BY CA CZ FI HU JP KP KR KZ LV NO NZ PL RO RU SK UA UZ
AU 9455627 A 940608 (9435)
EP 669978 A1 950906 (9540) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
CN 1094445 A 941102 (9543)
ADT WO 9411499 A1 WO 93-EP3191 931115; AU 9455627 A AU 94-55627 931115; EP 669978 A1 WO 93-EP3191 931115, EP 94-900810 931115; CN 1094445 A CN 93-115345 931113
FDT AU 9455627 A Based on WO 9411499; EP 669978 A1 Based on WO 9411499
PRAI US 92-975750 921113; US 93-38596 930326
AN 94-183501 [22] WPIDS
AB WO 9411499 A UPAB: 940722
A recombinant DNA vector (1) contg. a nucleotide sequence encoding Flk-1, a receptor for vascular endothelial growth factor (VEGF), is new. The Flk-1 gene is operatively associated with a regulatory sequence that controls gene expression in a host.

Also claimed are: (1) a vector (II) as above but encoding an Flk-1 fusion protein; (2) an engineered bost cell or cell lines contg. (I) or (II); (3) an isolated Flk-1 receptor protein; (4) a fusion protein comprising Flk-1 linked to a heterologous protein or peptide sequence; (5) an oligonucleotide encoding an antisence sequence complementary to a portion of the Flk-1 sequence,. which inhibits translation of the Flk-1 gene in a cell; (6) a monoclonal antibody (MAb) which is immunospecific for an epitope of Flk-1; (7) a VEGF agonist which is a MAb specific for an eptiope of Flk-1; (8) a recombinant vector (III) contg. a nucleotide sequence encoding a truncated Flk-q which has dominant negative acitivity which inhibits the cellular effects of VEGF bindng; (9) an engineered cell line contg. (III) which expresses truncated Flk-1; (10) an engineered cell line contg. (III) which produces infectious retrovirus particles expressing truncated Flk-1; (11) an isolated recombinant truncated Flk-1 which has dominant negative activity and which inhibits the cellular effects of VEGF binding.

USE - Flk-1 tyrosine **kinase** receptor expression has been found to be associated with endothelial cells and VEGF has been identified as a high affinity ligand of the receptor. The results indicate a major role for Flk-1 in the signalling system involved in vasculogenesis and angiogenesis. Pharmaceutical reagents designed to inhibit the Flk-1/VEGF interaction may be useful in inhibiting tumour growth. VEGF and/or VEGF agonists may be use to promote wound healing. The sol. Flk-1 receptor produced using the expression sytems described may be used to screen peptide libraries for molecules which inhibit the Flk-1/VEGF binding. The engineered cell lines of the invention, which express the receptor on their surface may be used to screen and identify VEGF against and antagonists. A transdominant negative form of the Flk-1 molecule has also been identified, which can be used to treat diseases resulting from abnormal proliferation of blood vessels, such as rheumatoid arthritis, retinopathies and growth of solid tumours.
Dwg.1/14

L7 ANSWER 11 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 93-086338 [11] WPIDS
DNC C93-038066
TI Use of mutated growth factor e.g. EGF receptors - for treatment of mammary, ovarian or lung carcinoma.
DC B04 D16
IN REDEMANN, N; **ULLRICH, A**; REDEMANN, N H; ULRICH, A; REDEMAN, N H
PA (PLAC) MAX PLANCK GES FOERDERUNG WISSENSCHAFTEN
CYC 40
PI DE 4129533 A1 930311 (9311)* 10 pp
WO 9305148 A1 930318 (9312) DE 43 pp
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA SE
W: AT AU BB BG BR CA CH CS DE DK ES FI GB HU JP KP KR LK LU MG MN MW NL NO PL RO RU SD SE
AU 9225185 A 930405 (9330)
CN 1071586 A 930505 (9409)
PT 100844 A 940531 (9421)
FI 9401053 A 940408 (9424)
NO 9400778 A 940504 (9427)

JP 07502884 W 950330 (9521)
NZ 244239 A 950726 (9535)
EP 667899 A1 950823 (9538) DE
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL SE
ADT DE 4129533 A1 DE 91-4129533 910905; WO 9305148 A1 WO 92-EP2058 920907; AU 9225185 A AU 92-25185 920907; CN 1071586 A CN 92-111396 920905; PT 100844 A PT 92-100844 920904; FI 9401053 A WO 92-EP2058 920907, FI 94-1053 940304; NO 9400778 A WO 92-EP2058 920907, NO 94-778 940304; JP 07502884 W WO 92-EP2058 920907, JP 93-504969 920907; NZ 244239 A NZ 92-244239 920907; EP 667899 A1 EP 92-918949 920907, WO 92-EP2058 920907
FDT AU 9225185 A Based on WO 9305148; JP 07502884 W Based on WO 9305148; EP 667899 A1 Based on WO 9305148
PRAI DE 91-4129533 910905
AN 93-086338 [11] WPIDS
AB DE 4129533 A UPAB: 931122
Claimed is a mutated growth factor receptor (R) as a medicament. The R pref. comprises (i) tyrosine **kinase** activity loss of the wild type receptor, (ii) a deletion in the domain of the tyrosine **kinase**, (iii) a deletion in the cytoplasmic domain of the tyrosine **kinase**, (iv) a mutated receptor tyrosine **kinase** i.e. mutatated epidermal growth factor receptor (E-R), (v) a point mutation at position 721 of E-R, pref. having alanine, (vi) E-R having a deletion of 533-C-terminal amino acids, or (vii) a point mutation of the wild type receptor.

Also claimed is a medicament having the receptors in liposomes or DNA fragments in recombinant retroviral viruses such as pNTK-HER-K721A and/or pNTK-HERCD-533 (DSM 6678 and DSM6679).

USE/ADVANTAGE - The medicament and the mutated receptor are used for the treatment of cancer, caused by over-production of Rs, such as breast, ovary and/or lung cancers (claimed). In contrast to prior art cancer treatments which involve interference with the DNA metabolism, the mutated receptors inhibit the transformation of an extra cellular growth signal so that it does not result in an intracellular growth signal. This effect was observed with co-expression of wild-type receptors
Dwg.0/3

L7 ANSWER 12 OF 12 WPIDS COPYRIGHT 1996 DERWENT INFORMATION LTD
AN 89-233846 [32] WPIDS
DNN N89-178288 DNC C89-104136
TI Treatment of tumour cells - by inhibiting growth factor receptor function with monoclonal antibody specifically HER2 receptor.
DC B04 D16 S03
IN HUDZIAK, R M; SHEPARD, H; **ULLRICH, A**
PA (GETH) GENENTECH INC
CYC 1
PI WO 8906692 A 890727 (8932)* EN 51 pp
W: JP
JP 03502885 W 910704 (9133)
ADT WO 8906692 A WO 89-US51 890105; JP 03502885 W JP 89-501807 890105
PRAI US 88-143912 880112; US 88-147461 880125
AN 89-233846 [32] WPIDS
AB WO 8906692 A UPAB: 930923
A monoclonal antibody (mAb1) specifically binding the extracellular

domain of the HER2 receptor is claimed. The antibody is capable of inhibiting the HER2 receptor function and of inhibiting serum activation of HER2 receptor function.

Also claimed is an assay for detecting a tumour comprising exposing cells to mAB1 and determining the extent of binding of the antibodies to the cells. Method of treating tumour cells comprises (1) administering an amt. of antibodies capable of inhibiting growth factor receptor function, and (2) administering a cytotoxic factor (I).

Also claimed is an assay for receptors and other proteins with increased tyrosine **kinase** activity comprising (a) exposing cells suspected to be TNF-x sensitive to TNF-x; (b) isolating those cells which are TNF-x resistant; (c) screening the isolated cells for increased tyrosine **kinase**, and (d) isolating receptors and other proteins having increased tyrosine **kinase** activity.

USE - MAb1 is useful for in vivo tumour therapy. Dosage is 0.1 -10mg/kg. The antibodies may be used for therapy of malignant or benign tumours where the abnormal growth rate of the tumour is dependent on growth factor receptors.

0/8

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ATHZ
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FILE COVERS 1967 - 20 Jun 1996  VOL 124 ISS 26
FILE LAST UPDATED: 20 Jun 1996  (960620/ED)

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  from the IPC subject headings and subheadings.


L14           2 SEA FILE=CAPLUS CIOSSEK T?/AU
L15         353 SEA FILE=CAPLUS ULLRICH A?/AU
L16           9 SEA FILE=CAPLUS MILLAUER B?/AU
L18           3 SEA FILE=CAPLUS MDK1/BI
L20           2 SEA FILE=CAPLUS (L14 OR L15 OR L16) AND L18

=> d bib ab l20 1-2

L20  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 1996 ACS
AN   1995:972773  CAPLUS
DN   124:82771
TI   Cloning, characterization, and differential expression of mouse
     developmental kinase MDK2 and MDK5, two novel receptor tyrosine
     kinases of the eck/eph family
AU   Clossek, Thomas; Lerch, Markus M.; Ullrich, Axel
CS   Department of Molecular Biology, Max-Planck-Institut fuer Biochimie,
     Martinsried, 82152, Germany
SO   Oncogene (1995), 11(10), 2085-95
     CODEN: ONCNES; ISSN: 0950-9232
DT   Journal
LA   English
AB   Using a polymerase chain reaction-based strategy for the cloning of
     developmentally regulated receptor tyrosine kinases, we identified
     two novel members of the eck/eph-related subfamily which, in analogy
     with the recently identified mouse developmental kinase 1 (
   MDK1), were designated MDK2 and MDK5.  MDK2 is highly
     homologous to the mouse kinase Myk-1 and the human kinase Htk,
     whereas MDK5 represents the mouse homolog of human Hek2.  Northern
     blot analyses of adult mouse tissues revealed a 4.7 kb transcript of
     MDK2 and a 4.8 kb transcript of MDK5 in various organ systems,
     including lung, liver, kidney, intestine, muscle hart, and, in the
     case of MDK5, also the brain.  In addn. to the full-length
     transcripts, smaller fragments were identified that probably
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represent truncated receptors. Northern blot anal. and in situ hybridization of mouse embryos indicated abundant expression during embryonic development, with preferential involvement of tissues of epithelial and endothelial origin for both kinases and of the spinal cord gray matter for MDK5. Unlike most other members of the eck/eph-related subfamily, the expression of MDK2 and MDK5 is not primarily restricted to neuronal structures, and their abundant presence in various organ systems during embryonic development suggests an important role ingestational growth and differentiation.

L20 ANSWER 2 OF 2 CAPLUS COPYRIGHT 1996 ACS
AN 1995:307905 CAPLUS
DN 122:183817
TI Identification of alternatively spliced mRNAs encoding variants of **MDK1**, a novel receptor tyrosine kinase expressed in the murine nervous system
AU **Ciossek, Thomas; Millauer, Birgit; Ullrich, Axel**
CS Department of Molecular Biology, Max-Planck-Institut fuer Biochemie, Martinsried, 82152, Germany
SO Oncogene (1995), 10(1), 97-108
CODEN: ONCNES; ISSN: 0950-9232
DT Journal
LA English
AB A novel member of the eck/eph family of receptor tyrosine kinases (RTKs), termed mouse developmental kinase 1 (**MDK1**), was identified and shown to be closely related to the Eek, Ehk1/Cek7, Ehk2, Cek4/Mek4/hek, and Sek/Cek8 subfamily. Northern blot anal. revealed **MDK1** mRNA transcripts of 6.8, 5.7, 4.0, 3.2, and 2.6 kb that encode apparent splice variants. Sequence analyses of **MDK1** cDNA clones from adult mouse brain predict the existence of .gtoreq.5 isoforms, including 2 truncated receptor variants lacking the kinase domain. Northern blot and in situ hybridization anal. indicate that in the adult mouse **MDK1** RNA expression is restricted to brain, testes, and spleen. The distinct patterns of **MDK1** gene expression during mouse development suggest an important role in the formation of neuronal structures and possibly other morphogenic processes.

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File  35:Dissertation Abstracts Online
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File 357:Derwent Biotechnology Abs 1982-1996/Jun B1
         (c) 1996 Derwent Publ Ltd
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         (c)1996 Royal Soc Chem & DECHEMA
File  73:EMBASE 1974-1996/Iss 23
         (c) 1996 Elsevier Science B.V.
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S2        999   AU=((ULLRICH, A?) OR (ULLRICH A?))
S3         29   AU=((MILLAUER, B?) OR (MILLAUER B?))
S4         10   MDK1 OR (MDK(W)1)
S5      80999   SIGNAL(W)TRANSDUC?
S6      36103   TYROSINE(W)KINASE? ?
S7          6   (S1 OR S2 OR S3) AND S4
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 11/7/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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09553237   96074837
 Cloning,  characterization, and differential expression of MDK2 and MDK5,
two novel receptor tyrosine kinases of the eck/eph family.
  ****Ciossek T****; Lerch MM; ****Ullrich A****
  Department of Molecular Biology, Max-Planck-Institut fur Biochemie,
Martinsried, Germany.
  Oncogene (ENGLAND)   Nov 16 1995,  11 (10) p2085-95,  ISSN 0950-9232
Journal Code: ONC
  Languages: ENGLISH
  Document type: JOURNAL ARTICLE
  Using a polymerase chain reaction-based strategy for the cloning of
developmentally regulated receptor tyrosine kinases,  we identified two
novel members of the eck/eph-related subfamily which, in analogy with the
recently identified mouse developmental kinase 1 (****MDK1****), were
designated MDK2 and MDK5. MDK2 is highly homologous to the mouse kinase
Myk-1 and the human kinase Htk, whereas MDK5 represents the mouse homologue
of human Hek2. Northern blot analyses of adult mouse tissues revealed a 4.7
kb transcript of MDK2 and a 4.8 kb transcript of MDK5 in various organ
systems, including lung, liver, kidney, intestine, muscle, heart, and, in
the case of MDK5, also the brain. In addition to the full-length
transcripts, smaller fragments were identified that probably represent
truncated receptors. Northern blot analysis and in situ hybridization of
mouse embryos indicated abundant expression during embryonic development,
with preferential involvement of tissues of epithelial and endothelial
origin for both kinases and of the spinal cord gray matter for MDK5. Unlike
most other members of the eck/eph-related subfamily, the expression of MDK2
and MDK5 is not primarily restricted to neuronal structures, and their
abundant presence in various organ systems during embryonic development
suggests an important role in gestational growth and differentiation.
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11/7/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09194729 95124729
Identification of alternatively spliced mRNAs encoding variants of ****MDK1**** , a novel receptor tyrosine kinase expressed in the murine nervous system.
****Ciossek T****; ****Millauer B****; ****Ullrich A****
Department of Molecular Biology, Max-Planck-Institut Fur Biochemie, Martinsried, Germany.
Oncogene (ENGLAND) Jan 5 1995, 10 (1) p97-108, ISSN 0950-9232
Journal Code: ONC
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A novel member of the eck/eph family of receptor tyrosine kinases (RTKs), termed mouse developmental kinase 1 (****MDK1****), was identified and shown to be closely related to the Eek, Ehk1/Cek7, Ehk2, Cek4/Mek4/hek and Sek/Cek8 subfamily. Northern blot analysis revealed ****MDK1**** mRNA transcripts of 6.8, 5.7, 4.0, 3.2 and 2.6 kb that encode apparent splice variants. Sequence analyses of ****MDK1**** cDNA clones from adult mouse brain predict the existence of at least five isoforms, including two truncated receptor variants lacking the kinase domain. Northern blot and in situ hybridization analysis indicate that in the adult mouse ****MDK1**** RNA expression is restricted to brain, testes and spleen. The distinct patterns of ****MDK1**** gene expression during mouse development suggest an important role in the formation of neuronal structures and possibly other morphogenic processes.
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